UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/479,783	01/07/2000	STANLEY T CROOKE	ISIS-4313	3541

7590 12/24/2003

Gwilm J. O. Attwell
1900 Market Street
Philadelphia, PA 19103

EXAMINER	
MCGARRY, SEAN	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 12/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

Office Action Summary	Application No.	Applicant(s)	
	09/479,783	CROOKE, STANLEY T	
	Examiner	Art Unit	
	Sean R McGarry	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 4 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 August 2003 and 21 August 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *43-46,68-82 and 89-116* is/are pending in the application.

4a) Of the above claim(s) *43-46,68-77,82,89-92 and 103-105* is/are withdrawn from consideration.

5)☒ Claim(s) *106* is/are allowed.

6)☒ Claim(s) *78-81,94-102 and 107-116* is/are rejected.

7)☒ Claim(s) *93* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *p12 2/14/0* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Attached to the instant Official Action is an initialed and signed copy of page 12 of 15 of the IDS filed 2/14/00. The remainder of the 15 pages were initialed and signed and provided to applicant in the Official Action mailed 5/01/03.

The drawings filed 8/21/03 have been received and are not objected to by the examiner.

Claims 43-46, 68-77, 89-92, and 103-105 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 13.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 78-81, and 94-102 remain and new claims 107-116 are rejected under 35 U.S.C. 102(b) as being anticipated by Agrawal et al [WO 94/01550]. This rejection is maintained for the reasons of record set forth in the Official Action mailed 5/01/03.

The instantly claimed invention is based on the observed target substrate for a dsRNase from T24 cells. The claimed invention is a double stranded RNA that comprises a first RNA having at least four consecutive ribofuranosyl residues having phosphodiester bonds and either of the oligonucleotides having modifications that allow increases nuclease resistance of increased substrate affinity including 2'methoxy modifications. The invention also reads on a double stranded RNA where both RNA oligonucleotide contain at least four consecutive ribofuranosyl residues. Further limitation includes that at least one of the oligonucleotides comprise from eight to fifty nucleoside units or comprise from 12 to 30nucleside subunits.

Agrawal et al have disclosed double stranded RNA duplexes. It has been disclosed that the double stranded RNAs comprise a targeting sequence and a self-complementary sequence (see page 8, for example). It has been disclosed at page 15, for example, that the self-complementary region can comprise 4 or more or 10 consecutive base pairing moieties and will generally be less than 50. It is disclosed at page 15, for example, that the regions can be connected by a non-nucleotide linker (i.e. 2 distinct oligonucleotide segments joined by a non-nucleotide linker). At page 16 it is disclosed that the self-complementary region can contain ribonucleotides and further one page 16 it has been disclosed the use of modifications such as 2'-o-Me ribonucleotides to hyper stabilize. It is also disclosed intercalating moieties (which clearly increase affinity between two complementary nucleic acids) at page 17, for example. At page 19 it has been disclosed both modifications for increasing nuclease resistance and for increased duplex stability. It has further been taught that the two

oligonucleotides can be a target RNA sequence and a ribozyme (see page 20 and Figure 7). See also figure 6. Agrawal et al have therefore disclosed all the limitations of the instantly claimed invention.

Claim 93 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The prior art does not teach a duplex RNA comprising SEQ ID NO: 8.

Claim 106 is allowed.

Applicant's arguments filed 8/4/03 have been fully considered but they are not persuasive.

In response to applicant's description of "The Present Invention" on page 13 of the response filed 8/4/03, which asserts the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e. three discrete entities that form the complex) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant argues that the prior art does not disclose "a double stranded RNA enzyme substrate. . ." It is noted that the prior art does not specifically disclose the

oligonucleotides as RNA enzyme substrates, however the prior art compounds meet all of the structural features of the claimed invention and are assumed, without evidence to the contrary to have the functional characteristics recited in the claims.

> **"[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted]." The burden of proof is similar to that required with respect to product-by-process claims. *In re Fitzgerald,* 619 F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (quoting *In re Best,* 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977)).**
>
> **MPEP 2112.01:**
>
> **PRODUCT AND APPARATUS CLAIMS — WHEN THE STRUCTURE RECITED IN THE REFERENCE IS SUBSTANTIALLY IDENTICAL TO THAT OF THE CLAIMS, CLAIMED PROPERTIES OR FUNCTIONS AREPRESUMED TO BE INHERENT**
>
> **Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433.**
>
> **COMPOSITION CLAIMS - IF THE COMPOSITION IS PHYSICALLY THE SAME, IT MUST HAVE THE SAME PROPERTIES**
>
> **"Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990)**

Applicant asserts that the Agrawal reference does not disclose modifications that increase resistance to single stranded nucleases and then describe some modifications disclosed in Agrawal et al that are not relied upon in the rejection. What applicants response does not address is that which is specifically relied upon, 2'-O-Me (2'methoxy

modifications) (see page 3 of the Official Action mailed 5/01/03). It is noted that this modification is specifically recited in applicants claims as being a modification that increases resistance to single stranded nucleases. It is unclear how the same modification would act as modification that increases resistance to single stranded nucleases in applicants claimed invention, but would not have that characteristic in the prior art. Applicant then argues the disclosure of intercalating agents disclosed by the prior art and asserts that intercalating agents do not provide resistance to single stranded nucleases. It is noted that applicant has not argued that these modifications offer added affinity to it partnered oligonucleotide, for example. Further applicant has baldly stated that intercalating agents are not chemical modifications. The intercalating agnets are cvhemical moieties that are attached to the oligonucleotide. Applicant has provided no evidence or argument that would show that these modifications are not chemical modifications. A review of the specification has failed to show a specific definition of "chemical modification" that would exclude intercalating agents, for example. At page 15 of applicant arguments applicant again argues many features not recited in the claims. Applicant, for example, asserts that the claimed inventin has no catalytic activity. Applicant is invited to point out where such activity is excluded. At the same page applicant asserts that the prior art is a ribozyme that catalysis the cleavage of a target, it is however noted that the ribozymes as disclosed by Agrawal have all of the structural characteristics of the claimed invention. Applicant argues that complexthe ribozymes of Agrawal et al are limited to the ribozyme and a target mRNA. This is simply not true and the Official Action has made that clear by pointing to figures7, for

example and discussing the double stranded RNAs that comprise a targeting region and a self-complementary region. At page 16 of applicant again argues limitations not present in the claims. Applicant asserts that target mRNA is not included in the claimed invention. The claims simply do not exclude mRNA as part of the complex. Applicant has added new claims that recite "a double stranded . . . wherein said first and second oligonucleotides are separate strands . . ." Applicant then argues that this means two unlinked oligonucleotides. This limitation does not exclude linked oligonucleotides. The claim limitation simply requires that the complex comprises to separate strands such as those oligonucleotide duplexes disclosed in Agrawal that comprise a non-nucleotide linker as set forth in the Official Action mailed 5/01/03. Two distinct oligonucleotide sequence linked by a non-nucleotide linker are still two separated, albeit linked, oligonucleotides. For example, if one ties two separate strands of thread to opposite ends of a paperclip, are the strands now not still separate strands of string?

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean R McGarry whose telephone number is (703)305-7028. The examiner can normally be reached on M-Th (6:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703) 308-0447. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

srm

SEAN McGARRY
PRIMARY EXAMINER
1635